Kidney International, Vol. 41 (1992), pp. 1064–1069

Ventilatory and metabolic changes during high efficiency hemodialysis

TOMMY SYMRENG, MICHAEL J. FLANIGAN, and VICTORIA S. LIM

Departments of Internal Medicine and Anesthesia, University of Iowa College of Medicine, Iowa City, Iowa, USA

Ventilatory and metabolic changes during high efficiency hemodialysis. Ventilatory and metabolic changes were measured in seven patients undergoing high efficiency hemodialysis using a cuprophane dialyzer and bicarbonate-containing dialysate. At an HCO_3 concentration of 35 mEq/liter and a mean in vivo urea clearance of 3.6 ml/kg/min, hypoxemia was not detected during dialysis (PaO_2 was 14.00 and 13.60 kPa before and during dialysis). The new findings, related to high efficiency bicarbonate dialysis, include a sustained rise in minute ventilation ($\dot{V}E$, 6.1 to 6.8 liter/min, $P < 0.01$), an increase in CO_2 excretion ($\dot{V}CO_2$, 194 to 214 ml/min, $P < 0.05$), and O_2 consumption ($\dot{V}O_2$, 215 to 246 ml/min, $P < 0.05$). The increment in $\dot{V}E$ and $\dot{V}CO_2$ was attributed to the high flux rate of bicarbonate while the rise in $\dot{V}O_2$ is likely the result of metabolic alkalosis. Arterial pH rose from 7.40 to 7.49 mm Hg and serum HCO_3 increased from 23.8 to 29.2 mEq/liter, while pCO_2 remained normal at 5.07 kPa throughout the study. The acid-base status of the blood changed from that of a metabolic acidosis to that of a respiratory acidosis across the dialyzer where the pH decreased from 7.47 to 7.41 and pCO_2 rose from 5.31 to 7.72 kPa. These data indicate that a healthy ventilatory response is needed to excrete the excess CO_2 generated during high efficiency bicarbonate hemodialysis. The significance and etiology of the elevated O_2 consumption is undetermined.

In the era of conventional hemodialysis, acetate was the buffer base in dialysate and hypoxemia the most prevalent respiratory change [1–5]. Such hypoxemia is primarily due to CO_2 loss across the dialyzer [6] with a minor contribution from an increasing alveolar-arterial oxygen gradient due presumably to leukocyte/platelet aggregates [2]. In this situation, hypoxemia is accompanied by reduced minute ventilation [7]. With the introduction of high efficiency hemodialysis and the use of bicarbonate buffer, there is a rapid flux of bicarbonate from the dialysate to the patient. We hypothesized that this flux would generate excess CO_2 and require an increase in ventilation to maintain acid-base balance. This report focuses on the ventilatory and metabolic changes of high efficiency hemodialysis.

Methods

Study subjects and dialysis treatment

Seven hemodialysis patients were recruited for this study, their demographic and clinical data are listed in Table 1. All participants were clinically stable and without intercurrent illness. There were four women and three men, their ages ranged from 20 to 55 years. Four patients had chronic glomerulonephritis, and one each had hypertensive nephrosclerosis, adult polycystic kidney disease, and medullary cystic kidney disease. No patient had diabetes mellitus. Medications consisted of phosphate binders and multivitamins; one subject (JD) received enalapril[R]. Renal replacement consisted of high efficiency hemodialysis using the Gambro Single Pass Delivery System with an ultrafiltration controller and bicarbonate dialysate. Dialysis was performed three times a week and three hours per session using new Gambro IC 6 N (1.6 m^2) dialyzers and bicarbonate dialysate ("Bicart," Cobe, Gambro, Hospal Inc., Na = 142 mEq/liter, K = 2 mEq/liter, Ca = 3.25 mEq/liter, Mg = 1 mEq/liter, Cl = 101.5 mEq/liter, acetic acid = 3 mEq/liter, dextrose = 200 mg%, HCO_3 = 38 mEq/liter). The commercially purchased dialysate contains 38 mEq/liter of bicarbonate and 3 mmol/liter of acetate; the bicarbonate concentration of the diluted dialysate, when measured, had a mean value of 35 mEq/liter. Blood flow rate was 400 ml/min and dialysate flow rate, 500 ml/min. Mean in vivo urea clearance derived from dialysate urea removal was 247 ml/min (range 194 to 274). This resulted in derivation of a mean dialysis adequacy index (Kt/V) of 1.16 using the single-pool variable-volume urea kinetics (range 0.71 to 1.77) and a mean normalized protein catabolic rate (NPCR) of 0.98 g/kg/day (range 0.67 to 1.41). Both Kt/V and NPCR were calculated from the dialysis preceeding the experiment. Study dialyses were performed as described but dialysis was shortened to two and one half hours.

Experimental design

Subjects were admitted to the Clinical Research Center and studied the next morning after a 12 hour fast. Ventilation, expired gas collections, and arterialized blood (obtained from the arteriovenous fistula) samples were obtained every 30 minutes beginning two hours before and ending four hours after completion of dialysis. Partial pressures of CO_2 and O_2 were determined in blood and gas samples, and pH and HCO_3 were measured in blood samples.

Acute changes in acid-base status across the dialyzer were examined by measuring pH, PCO_2 and HCO_3 in blood and dialysate samples obtained simultaneously proximal and distal to the dialyzer at 60 and 120 minutes during dialysis in four subjects. Transfer of CO_2 in gaseous form across the dialyzer was calculated from the following [8, 9]:

Received for publication June 27, 1991
and in revised form October 4, 1991
Accepted for publication October 7, 1991

Table 1. Demographic and dialysis status of the study subjects

Subject	Age/sex	Ht/wt *m/kg*	Kt/V	NPCR *g/kg/day*
IA	56/F	1.61/76.7	1.31	0.98
JD	32/M	1.93 76.5	0.71	0.77
EB	54/F	1.64/83.6	1.36	1.41
TD	23/F	1.53/40.3	1.77	1.14
RF	46/M	1.81/87.8	0.86	0.97
VM	39/F	1.60/55.8	1.11	0.81
RS	20/M	1.68/54.5	1.02	0.94

Kt/V is dialysis adequacy index calculated by single compartment variable volume kinetics, and NPCR is protein catabolic rate normalized for a standard urea volume of 58% of body weight, as follows: NPCR = PCR/ (V/0.58).

$$CO_2 \text{ (mmol/liter)} = (\Delta pCO_2/BP) \times (0.533/25.6)$$

Where ΔpCO_2 is difference in CO_2 tension across the dialyzer, BP is the barometric pressure (STPD), 0.533 is the CO_2 solubility coefficient, and 25.6 is Avogadro's constant stating that one mole of CO_2 occupies a volume of 25.6 liters at 38°C.

The protocol was approved by the Committee on Human Research of the University of Iowa College of Medicine.

Indirect calorimetry

Respiratory gas exchange, including O_2 consumption and CO_2 production, was determined by a portable metabolic Gas Monitor (MGM II, Utah Medical Products, Midvale, Utah, USA). During measurement, a mouth piece attached to a two-way valve was used. Expired gas was sampled by a small gas line leading from the mouth piece to a zirconium-oxide O_2 analyzer and an infra-red CO_2 sensor. Simultaneously, tidal volume and frequency of respiration were recorded by a pneumotacograph and an ultrasonic flow transducer. Partial pressures of the inspired O_2 and CO_2 were derived from the atmosphere. $\dot{V}E$, $\dot{V}O_2$ and $\dot{V}CO_2$ were calculated by standard equations and corrected for STPD. Before each experiment, the equipment was calibrated with a reference gas standard consisting of 21% O_2 and 10% CO_2 and the flow transducer was checked by a calibrated syringe [10, 11].

Data were stored in the clinfo system and were examined by one-way analysis of variance and Duncan's multiple comparison test as well as paired *t*-test when appropriate.

Results

Figure 1 and Table 2 summarize ventilatory changes during high efficiency hemodialysis. Minute ventilation increased from a baseline of 6.1 to 6.8 liter/min within 30 minutes after initiating dialysis and remained elevated during and for four hours following dialysis. Similarly, CO_2 production ($\dot{V}CO_2$) increased from a basal value of 194 ml/min to 214 and 218 ml/min during and after dialysis, respectively. Oxygen consumption ($\dot{V}O_2$) which was 215 ml/min in the basal state, rose to 226 and 246 ml/min during and after dialysis, respectively.

Figure 2 and Table 3 depict changes in the patient's acid-base parameters. Initiating dialysis resulted in a prompt rise in pH, from 7.40 to 7.48 and 7.49 during and after dialysis, respectively. Likewise serum bicarbonate rose from 24 mEq/liter pre-dialysis to 29 mEq/liter during and after dialysis. In the face of significant alkalosis, pCO_2 remained normal and remarkably stable at 5.07 to 5.20 kPa throughout the observation period. Arterial oxygen tension (pO_2) which was normal (14.00 kPa) before dialysis, remained so (13.60 kPa) during dialysis, but was reduced to 11.73 kPa three to four hours following dialysis. Despite the reduced oxygen tension, O_2 saturation remained excellent at 97%. The $(A\text{-}a)O_2$ gradient (Table 3) which was 5.6 mm Hg in the pre-dialysis period, rose modestly and progressively to 12.1 mm Hg during and 16.5 mm Hg at the end of the study. It should be noted that only one of our study subjects had a pre-dialysis serum bicarbonate level below 23 mEq/liter and arterial pH was equal to or above 7.35 in all.

Table 4 and Figure 3 summarize and depict acid-base changes across the dialyzer. Dialysis against a delivered bicarbonate concentration of 35 mEq/liter resulted in a marked rise in pCO_2 (kPa) from 5.31 in the arterial blood entering the dialyzer to 6.72 in the venous blood returning to the patient. Serum bicarbonate (mEq/liter) increased from 29 in the arterial inlet to 32 in the venous outlet. Because the rise in pCO_2 was proportionately greater than that of the bicarbonate, the pH of the blood returned to the patient was reduced to 7.41, while the systemic arterial pH was 7.47. Analysis made in the dialysate compartment showed diametric changes; HCO_3 was reduced from 34.8 to 32 mEq/liter and pCO_2 from 8.30 to 6.52 kPa, causing the dialysate to become more alkaline as it passed through the dialyzer.

During dialysis, patients gained CO_2, from CO_2 dissolved in the dialysate at a rate of 0.24 mmol/min or 6.3 ml/min. While the pCO_2 difference across the dialyzer was constant throughout dialysis, the HCO_3 gradient across the dialyzer was not; it was large in the beginning and fell with time. During its passage through the dialyzer, the blood gained O_2 from the dialysate; the amount transferred was, however, less than 3 ml/min, calculated from hemoglobin level, O_2 saturation and pO_2.

Discussion

When acetate is used as the buffer base during hemodialysis, the fall in arterial oxygen pressure is usually modest, ranging from 10 to 15% of baseline value, though arterial pO_2 may be reduced to as low as 9.33 kPa in subjects without pulmonary disease. The prevailing view believes that such hypoxemia is largely the result of CO_2 and bicarbonate loss across the dialyzer with secondary reduction in minute ventilation. This concept is supported by abundant data showing a reduction in pCO_2 and $\dot{V}CO_2$ during dialysis [6, 7, 12–16] and elimination [17–21] or attenuation [22, 23] of dialysis-induced hypoxemia by substituting bicarbonate for the acetate buffer. There are, however, reports showing significant pO_2 reductions with bicarbonate dialysate [12–16]. The reason for such discrepancy is not clear. In the current study, we found that bicarbonate dialysate obviated the development of hypoxemia during hemodialysis despite use of a complement-activating membrane. This underscores CO_2 loss as the primary cause of hypoxemia associated with acetate dialysate and minimizes the role of ventilation/perfusion mismatching or shunt resulting from altered pulmonary perfusion.

The minimal reduction in pO_2 to 11.73 kPa following completion of dialysis in our patients could not be explained by abnormal ventilation since the dead space to tidal volume ratio remained constant, nor on the basis of respiratory suppression by metabolic alkalosis because there was no evidence of

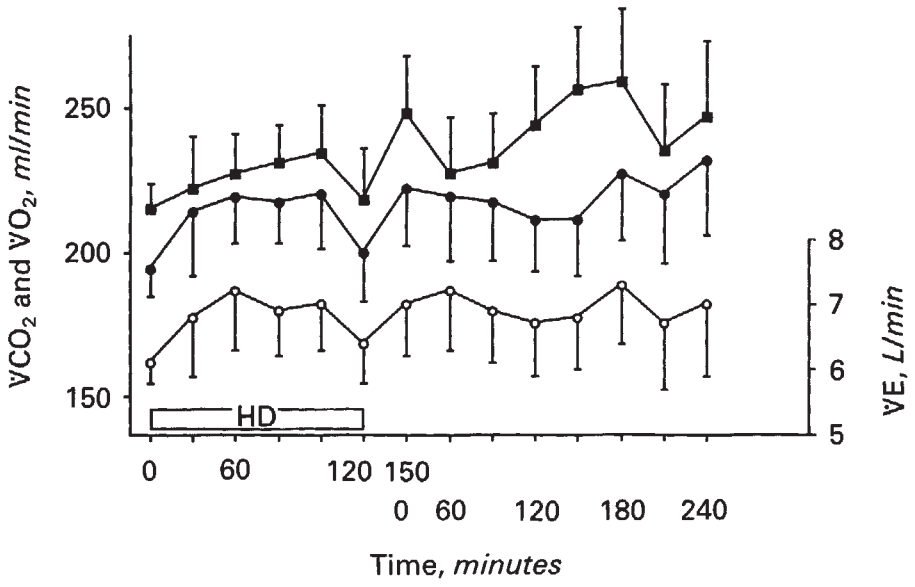

Fig. 1. *Ventilatory changes during high efficiency hemodialysis.* Values are depicted as means ± SEM. Hemodialysis led to an increase in minute ventilation [$\dot{V}E$, ⊖] and CO_2 excretion [$\dot{V}CO_2$, ●]. O_2 consumption [$\dot{V}O_2$, ■] was increased in the post-dialysis period.

Table 2. Ventilatory changes associated with high efficiency hemodialysis

Period	$\dot{V}CO_2$	$\dot{V}O_2$	$\dot{V}E$	$\dot{V}CO_2/\dot{V}O_2$
	ml/min		*liter/min*	
Pre-HD	194 ± 47	215 ± 47	6.11 ± 1.75	0.90 ± 0.10
HD	214 ± 45[a]	226 ± 40	6.86 ± 1.93[b]	0.94 ± 0.09
Post-HD	218 ± 51[a]	246 ± 52[a]	6.89 ± 2.13[a]	0.89 ± 0.10
ANOVA DF	115			
F	2.40	4.43	1.60	3.03
P	0.095	0.014	0.207	0.05

All values are listed as means ± SD, $\dot{V}CO_2$, $\dot{V}O_2$ and $\dot{V}E$ represent, respectively, CO_2 excretion, oxygen consumption and minute ventilation. Pre-HD, HD, and Post-HD represent the mean of each subject's mean pre- ($N = 5$), intra- ($N = 5$), and post-dialysis ($N = 8$) values. In the analysis of variance, degree of freedom (DF), F and *P* values are listed for each parameter. [a] and [b] represent, respectively, *P* values of < 0.05 and < 0.01 comparing HD and post-HD to pre-HD values by paired *t*-test.

hypoventilation. In fact, minute ventilation was increased and pCO_2 remained normal. Hunt and colleagues also noted persistent hypoxemia post-dialysis and postulated several potential mechanisms, including intra-pulmonary leukostasis, decreased cardiac output and micro-atelectasis [11]. The time course of this hypoxemia is inconsistent with complement activated leukostasis which occurs within 30 to 60 minutes of dialysis initiation. The late and prolonged fall of pO_2 associated with a rising arterial to alveolar oxygen gradient is most consistent with the hypothesis that micro-atelectasis of recumbency rather than dialysis causing the fall in pO_2. Most patients undergoing this type of study are recumbent; our study subjects specifically had been in bed for sixteen hours by the experiments' completion. The increase in $(A\text{-}a)O_2$ gradient from a baseline of 6 to 16 mm Hg post-dialysis is consistent with such speculation, nonetheless, the possibility of a delayed onset of ventilation/perfusion mismatch cannot be excluded.

The respiratory exchange ratio is generally reduced with acetate and normal with bicarbonate dialysate [7, 14, 15]. The former is, in part, due to an increased oxygen consumption associated with acetate metabolism [24]. By contrast, we found a significant rise in the respiratory quotient during dialysis and we are attributing this increase to oxidative metabolism of dialysate glucose.

As expected, hemodialysis increased the serum bicarbonate concentration and the blood pH. Despite enormous shifts in pH and HCO_3, pCO_2 remained normal with virtually no fluctuation throughout the study period (Fig. 2). This observation stresses the exquisite sensitivity of the respiratory center in regulating pCO_2. The absolute HCO_3 gain is difficult to quantitate because bicarbonate space is not static during and immediately post-dialysis and because a significant amount of bicarbonate is lost through ultrafiltration.

While arterial pCO_2, CO_2 production rate, and minute ventilation are reduced with acetate-containing dialysate, they are generally reported to be normal when bicarbonate is substituted for acetate [7, 12, 14, 15, 18]. In the current study, we found that the combination of bicarbonate dialysate and high efficiency hemodialysis generated substantial quantities of CO_2 gas which then stimulated respiration as evidenced by a 13% increase in minute ventilation ($\dot{V}E$) and CO_2 production. We believe the rise in $\dot{V}CO_2$ is primarily due to bicarbonate metabolism and subsequent CO_2 generation, not transfer of dissolved CO_2 from the dialysate [25]. The calculated gain of gaseous CO_2 (Table 4, blood compartment) was only 0.13 mmol/min or 3.3 ml/min, which was 1.7% of the basal CO_2 production rate. It should be emphasized that the increase in $\dot{V}CO_2$ and $\dot{V}E$ persisted for at least four hours following completion of hemodialysis. Since alkalosis generally inhibits respiration, the need to acutely excrete excess CO_2 delivered during dialysis apparently overrode this inhibition. This suggests that the need to excrete the excess CO_2 takes precedence over the need to maintain a normal pH. Alternatively, the lack of respiratory inhibition during bicarbonate dialysis may, in part, be due to the relative difficulty with which bicarbonate penetrates blood-brain and cellular barriers allowing CO_2 to

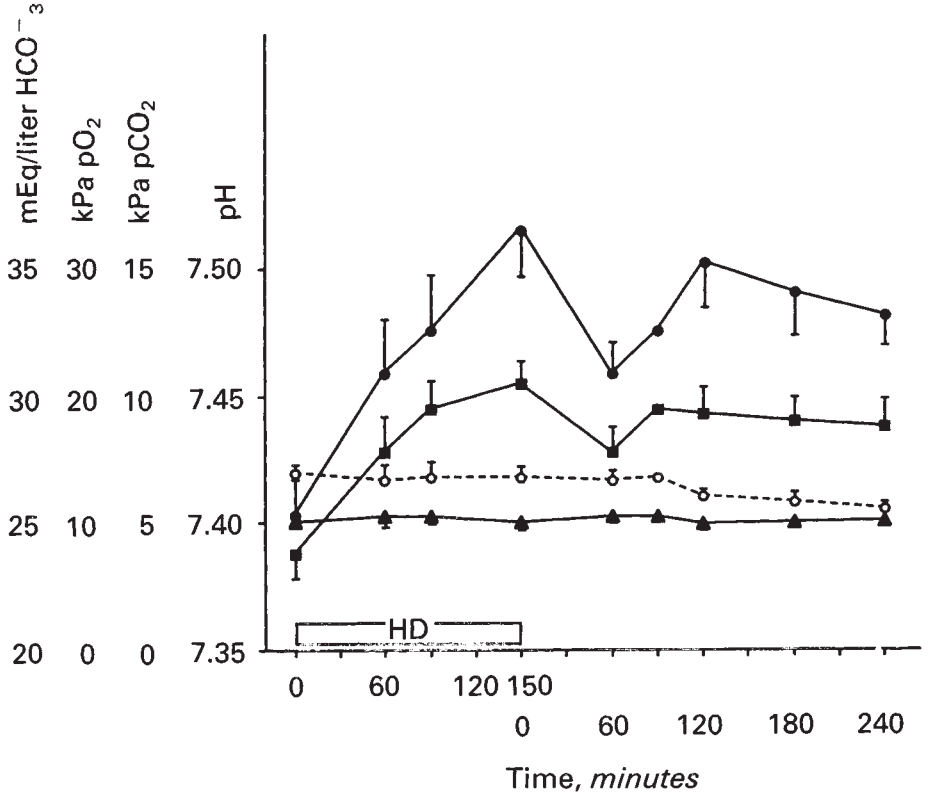

Fig. 2. *Changes in acid-base status during high efficiency hemodialysis.* Values are presented as means ± SEM. Hemodialysis resulted in an increase in arterial pH (●) and serum HCO_3 (■); pCO_2 (▲), however, remained normal, and pO_2 (○) was slightly reduced in the post-dialysis period.

Table 3. Changes in arterial blood gases with high efficiency hemodialysis

Period	pH	pCO_2	pO_2	HCO_3	% Sat	$(A - a)O_2$
		mm Hg		*mEq/L*		*mm Hg*
Pre-HD	7.404 ± 0.049	38 ± 3	105 ± 16	23.8 ± 3.4	97.7 ± 1.1	5.63 ± 7.20
HD	7.484 ± 0.057[a]	39 ± 3	102 ± 23	29.2 ± 3.1[a]	97.8 ± 1.2	12.09 ± 10.68
Post-HD	7.494 ± 0.038[a]	38 ± 3	88 ± 14[a]	29.2 ± 2.6[a]	97.0 ± 1.4	16.46 ± 12.75
ANOVA DF	60					
F	15.92	0.37	5.36	16.29	2.39	3.95
P	0.003×10^{-3}	0.69	0.007	0.002×10^{-3}	0.100	0.02

All values are means ± SD. Results of analysis of variance, including degree of freedom, F and *P* values are listed under each parameter. $(A - a)O_2$ indicates alveolar-arterial pO_2 gradient or $PAO_2 - PaO_2$. $PAO_2 = PiO_2 - PaCO_2 \times \{FiO_2 + [(1 - FiO_2)/R]\}$

[a] $P < 0.01$ by paired *t*-test comparing the mean of the intra- and post-dialysis values to the mean of the pre-dialysis values

diffuse into these cells and produce an intracellular acidosis [26, 27] in the presence of an extracellular alkalosis.

Changes in acid-base status across the dialyzer, including influx of bicarbonate and dissolved CO_2 into the blood, are predictable. The change in pH was unexpected; blood returning to the patient was more acidic than that entering the dialyzer, and the spent dialysate was more alkaline than the fresh solution. These paradoxes were best explained by the preponderant or greater magnitude of change in pCO_2 versus bicarbonate. Thus, blood enters the extracorporeal circuit with findings of a metabolic acidosis, and is returned to the patient with values reflecting a respiratory acidosis.

It is important to emphasize that an adequate ventilatory capacity is imperative to excrete the excess CO_2 generated during high efficiency bicarbonate hemodialysis. In patients whose respiratory function is compromised or in whom ventilation is fixed during mechanical ventilation, bicarbonate loading poses the risk of hypercarbia and respiratory acidosis. While Bouffard et al did not find an elevated pCO_2 during bicarbonate dialysis in sedated, mechanically ventilated patients [28], their study permitted wide variations in minute ventilation, and the dialysate bicarbonate concentration was much lower than that currently in use. Moreover, their dialysis efficiency was probably lower than that achieved by high efficiency hemodialysis. Further increases in dialysis efficiency will accentuate the acid-base disturbances of rapid bicarbonate administration and may precipitate transient respiratory acidosis.

Increased oxygen consumption with hemodialysis is generally reported with acetate [24], but not recognized with bicarbonate dialysate. We are attributing the rise in $\dot{V}O_2$ observed in our subjects to the development of a metabolic alkalosis.

Table 4. Acid-base changes across the dialyzer analyzed from blood and dialysate compartments

Site	N	pH	pCO_2	pO_2	HCO_3	CO_2 gain	HCO_3 gain *mmol/min*	
			mm Hg		*mEq/liter*	*mmol/min*	60 min	120 min
B/afferent	8	7.466 ± 0.033	39.8 ± 2.9	87.6 ± 11.1	29.0 ± 2.8	0.130 ± 0.534	0.319 ± 0.534	0.184 ± 0.304
B/efferent	8	7.410 ± 0.036	50.4 ± 2.6	97.2 ± 10.6	32.2 ± 1.4			
P		0.0001	0.0001	0.004	0.002			
D/afferent	8	7.357 ± 0.077	62.3 ± 11.1	127.5 ± 6.0	34.8 ± 0.6	−0.240 ± 0.146	−0.660 ± 1.223	−0.309 ± 0.561
D/efferent	8	7.432 ± 0.115	48.9 ± 14.1	115.1 ± 16.1	32.0 ± 2.1			
P		0.121	0.033	NS	0.005	NS	NS	

All values are listed as means ± SD. B/afferent and B/efferent and D/afferent and D/efferent indicate blood and dialysate entering and leaving the dialyzer, respectively. *P* indicates *P* value by paired *t*-test.

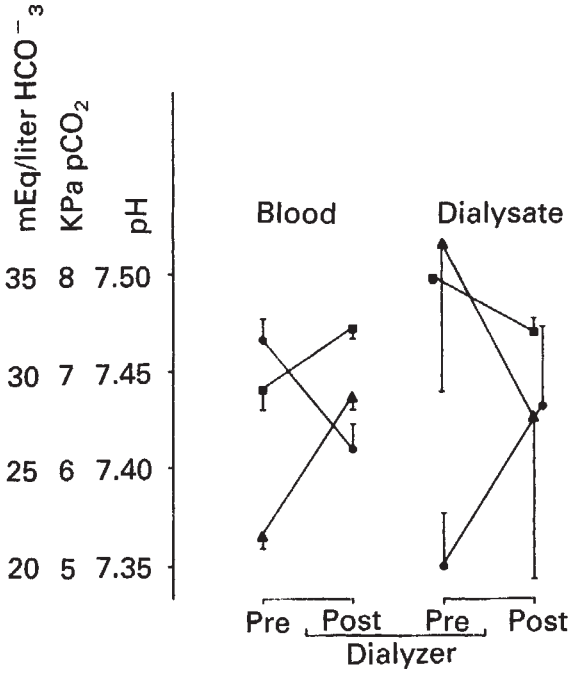

Fig. 3. *Changes in acid-base status across the dialyzer.* In the blood compartment, HCO_3 (■) and pCO_2 (▲) rose whereas pH (●) decreased. By contrast, in the dialysate compartment, HCO_3 and pCO_2 were reduced, and pH actually rose.

Arterial pH rose from 7.40 in the baseline to 7.48 and 7.49 during and after dialysis. High oxygen uptake during hyperventilation is well recognized [29–31]. This increase in oxygen consumption is independent of the mechanical work of breathing, since it is observed in subjects whose respiratory muscles are paralyzed and who are ventilated mechanically. It is believed that a fall in intracellular hydrogen concentration leads to enhanced ATP hydrolysis and oxidative metabolism by stimulating the activity of phosphofructokinase, the rate-limiting enzyme involved in the glycolytic pathway rather than stimulating lactate production [32, 33]. The physiologic significance of this increase in oxygen consumption associated with high efficiency dialysis is yet to be determined.

In summary, similar to other studies, we note that using bicarbonate dialysate eliminated hypoxemia. With regard to ventilation, we found significant increases in minute ventilation and CO_2 excretion. Such increments are best explained by the bicarbonate flux from the dialysate to the patient and the subsequent CO_2 generation following bicarbonate neutralization. This increased CO_2 production would lead to hypercarbia if a compensatory rise in minute ventilation ($\dot{V}E$) did not occur. Failure of alkalosis to suppress respiration may, in part, be explained by the difficulty with which bicarbonate penetrates cellular and blood brain barriers. Metabolic alkalosis, nevertheless, resulted in increased oxygen consumption, a phenomenon that is not generally recognized in dialysis patients.

Acknowledgments

This work was supported by Baxter's Extramural Grant Program, an award from Gambro, USA, and Grant RR55 of the General Research Center Program, NIH. We thank the staff of the Dialysis Unit and the Clinical Research Center for patient care, Jerry Fangman, David Tatman and James Starr for technical assistance, and Sarah Parker for secretarial help.

Reprint requests to Victoria S. Lim, M.D., Department of Internal Medicine, University of Iowa Hospitals, Iowa City, Iowa 52242, USA.

References

1. Craddock PR, Fehr J, Brigham K, Kronenberg RS, Jacob HS: Complement and leukocyte-mediated pulmonary dysfunction in hemodialysis. *N Engl J Med* 296:769–774, 1977
2. Craddock PR, Fehr J, Dalmasso AP, Brigham L, Jacob HS: Hemodialysis leukopenia: Pulmonary vascular leukostasis resulting from complement activation by dialyzer cellophane membranes. *J Clin Invest* 59:879–888, 1977
3. Kraut JA, Gaffer U, Miller JH, Shinaberger JH: Prevention of arterial hypoxemia during dialysis by use of bicarbonate dialysate. (abstract) *Kidney Int* 14:678, 1978
4. Jacob AI, Gavellas G, Zarco R, Perez G, Bourgoigne JJ: Leukopenia, hypoxia and complement function with different hemodialysis membranes. *Kidney Int* 18:505–509, 1980
5. Dumler R, Levin NW: Leukopenia and hypoxemia: Unrelated effects of hemodialysis. *Arch Intern Med* 139:1103–1106, 1979
6. Aurigemma NM, Feldman NT, Gottlieb M, Ingram RH Jr, Lazarus JM, Lowrie EG: Arterial oxygenation during hemodialysis. *N Engl J Med* 297:871–873, 1977
7. Dolan MJ, Whipp BJ, Davidson WD, Weitzman RE, Wasserman K: Hypopnea associated with acetate hemodialysis: Carbon dioxide-flow-dependent ventilation. *N Engl J Med* 305:72–75, 1981
8. Eiser AR, Jayamanne D, Kokseng C, Che H, Slifkin RF, Neff MS: Contrasting alterations in pulmonary gas exchange during acetate and bicarbonate hemodialysis. *Am J Nephrol* 2:123–127, 1982
9. Hampl H, Klopp H, Wolfgruber M, Pustelnik A, Schiller R, Hansfeld F, Kessel M: Advantages of bicarbonate hemodialysis. *Artif Organs* 6:410–416, 1982
10. Abu-Hamdan DK, Desai SG, Mahajan SK, Muller BF, Briggs WA, Lynne-Davies P, McDonald FD: Hypoxemia during hemodialysis using acetate versus bicarbonate dialysate. *Am J Nephrol* 4:248–253, 1984

11. HUNT JM, CHAPPELL TR, HENRICH WL, RUBIN LJ: Gas exchange during dialysis. *Am J Med* 77:255–260, 1984
12. HENRICH WL, WOODARD TD, MEYER BD, CHAPPELL TR, RUBIN LJ: High sodium bicarbonate and acetate hemodialysis: Double-blind crossover comparison of hemodynamic and ventilatory effects. *Kidney Int* 24:240–245, 1983
13. SEVERINGHAUS JW, STUPFEL M, BRADLEY AF: Accuracy of blood pH and P_{CO_2} determinations. *J Appl Physiol* 9:189–196, 1956
14. SEVERINGHAUS JW, STUPFEL M, BRADLEY AF: Variations of serum carbonic acid pK with pH and temperature. *J Appl Physiol* 9:197–200, 1956
15. JEQUIER E: Direct and indirect calorimetry in man (chapt 9), in *Substrate and Energy Metabolism*, edited by GARROW JS, HALLIDAY D, LIBBEY J, 1985, pp. 82–92
16. WESTENSKOW DR, CUTLER CA, WALLACE WD: Instrumentation for monitoring gas exchange and metabolic rate in critically ill patients. *Crit Care Med* 12:183–187, 1984
17. VANSTONE JC, COOK J: The effect of bicarbonate dialysate in stable chronic hemodialysis patients. *Dial Transplant* 8:703–704, 1979
18. IGARASHI H, KIOI S, GEJYO F, ARAKAWA M: Physiologic approach to dialysis-induced hypoxemia. *Nephron* 41:62–69, 1985
19. LEUNISSEN KML, HOORNTJE SJ, FIERS HA, DEKKERS WT, MULDER AW: Acetate versus bicarbonate hemodialysis in critically ill patients. *Nephron* 42:146–151, 1986
20. DALAL S, YU AW, GUPTA DK, KAR PM, ING TS, DAUGIRDAS JT: L-Lactate high-efficiency hemodialysis: Hemodynamics, blood gas changes, potassium/phosphorus, and symptoms. *Kidney Int* 38: 896–903, 1990
21. TOLCHIN N, ROBERTS JL, LEWIS EJ: Respiratory gas exchange by high-efficiency hemodialyzers. *Nephron* 21:137–145, 1978
22. DEBACKER WA, VERPOOTEN GA, BORGONJON DJ, VERMEIRE PA, LINS RR, DEBROE ME: Hypoxemia during hemodialysis: Effects of different membranes and dialysate compositions. *Kidney Int* 23: 738–743, 1983
23. HAKIM RM, PONTZER M-A, TILTON D, LAZARUS JM, GOTTLIEB MN: Effects of acetate and bicarbonate dialysate in stable chronic dialysis patients. *Kidney Int* 28:535–540, 1985
24. OH MS, URIBARRI J, DELMONTE ML, HENEGHAN WF, KEE CS, FRIEDMAN EA, CARROLL HJ: A mechanism of hypoxemia during hemodialysis. *Am J Nephrol* 5:336–371, 1985
25. SARGENT JA, GOTCH FA: Bicarbonate and carbon dioxide transport during hemodialysis. *ASAIO J* 2:61–72, 1979
26. SHAPIRO JI, WHALEN M, KUCERA R, KINDIG N, FILLEY G, CHEN L: Brain pH responses to sodium bicarbonate and carbicarb during systemic acidosis. *Am J Physiol* 256:H1316–H1321, 1989
27. ARIEFF AI, LEACH W, PARK R, LAZAROWITZ VC: Systemic effects of $NaHCO_3$ in experimental lactic acidosis in dogs. *Am J Physiol* 242:F586–F591, 1982
28. BOUFFARD Y, VIALE J-P, ANNAT G, GUILLAUME C, PERCIVAL C, BERTRAND O, MOTIN J: Pulmonary gas exchange during hemodialysis. *Kidney Int* 30:920–923, 1986
29. CAIN SM: Increased oxygen uptake with passive hyperventilation of dogs. *J Appl Physiol* 28(1):4–7, 1970
30. KHAMBATTA HJ, SULLIVAN SF: Effects of respiratory alkalosis on oxygen consumption and oxygenation. *Anesthesiology* 35:53–58, 1973
31. BRICE AG, WELCH HG: Effect of respiratory alkalosis on skeletal muscle metabolism in the dog. *J Appl Physiol* 58(2):658–664, 1985
32. HINDMAN BJ: Sodium bicarbonate in the treatment of subtypes of acute lactic acidosis: Physiologic considerations. *Anesthesiology* 72:1064–1076, 1990
33. GOTCH FA, SARGENT JA, KEEN ML: Hydrogen ion balance in dialysis therapy. *Artif Organs* 6(4):388–395, 1982